

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) An oral pharmaceutical formulation comprising at least one bisphosphonate and one or more of an additive agent, said additive agent being present in an amount between 80% to 99.9% by weight of the formulation [sufficient] to provide an enhanced absorption of the bisphosphonate, and said additive being selected from the group consisting of
- a surfactant;
 - an ampholytic surfactant;
 - an anionic surfactant;
 - a cationic surfactant;
 - a bile salt;
 - a soap and a fatty acid, and a salt thereof;
 - a lipid with the exception of a medium chain glyceride or a mixture of medium chain glycerides;
 - an oil;
 - an enamine;
 - a chelating agent;
 - a phenothiazine;
 - a fatty acid derivative of carnitine or a peptide;
 - a substance selected from the group consisting of azone, concanavalin A, a phosphate and a phosphonate derivative;
 - a product of a Maillard reaction;
 - a polymer;
 - a chitosan and a chitosan derivative; and
 - combinations thereof.

2. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a nonionic surfactant.
3. (Previously presented) The pharmaceutical formulation according to claim 2, wherein the nonionic surfactant is a sugar glycoside or a sugar fatty acid ester.
4. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a lipid.
5. (Previously presented) The pharmaceutical formulation according to claim 4, wherein the lipid is a phospholipid.
6. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is an oil.
7. (Previously presented) The pharmaceutical formulation according to claim 6, wherein the oil is soy bean oil or sunflower oil.
8. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a chelating agent.
9. (Previously presented) The pharmaceutical formulation according to claim 8, wherein the chelating agent is EDTA, EGTA or citric acid.
10. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a fatty acid derivative of carnitine or a peptide.
11. (Previously presented) The pharmaceutical formulation according to claim 10, wherein the additive of the fatty acid derivative of carnitine or a peptide is palmitoyl-DL-carnitine.

12. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a polymer.
13. (Previously presented) The pharmaceutical formulation according to claim 12, wherein the polymer is a polyacrylic acid.
14. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a block copolymer.
15. (Previously presented) The pharmaceutical formulation according to claim 14, wherein the block copolymer is a poloxamer, a poloxamine or meroxapol.
16. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a saponin.
17. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a biodegradable polymer.
18. (Previously presented) The pharmaceutical formulation according to claim 17, wherein the biodegradable polymer is polyactid acid or polyglycolic acid.
19. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a combination of a lipid and a surfactant.
20. (Previously presented) The pharmaceutical formulation according to claim 19, wherein the combination of the lipid and the surfactant is monoolein and sodium taurocholate, or monoolein and Tween 80.

21. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a combination of a lipid of non-phospholipid character and a phospholipid.

Claim 22 (Canceled)

23. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a combination of a lipid and a block copolymer.

24. (Previously presented) The pharmaceutical formulation according to claim 23, wherein the combination of the lipid and the block copolymer is monoolein and Pluronic F 127.

25. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a combination of a surfactant and an oil.

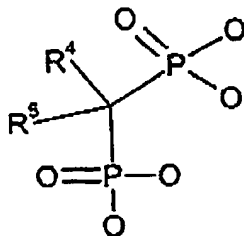
26. (Previously presented) The pharmaceutical formulation according to claim 25, wherein the combination of the surfactant and the oil is a sucrose fatty acid ester and soy bean oil.

27. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a combination of a polymer and a lipid.

28. (Previously presented) The pharmaceutical formulation according to claim 27, wherein the combination of the polymer and the lipid is polycarbophil and monoolein.

29. (Previously presented) The pharmaceutical formulation according to claim 1, wherein said additive is in the form of an emulsion or a microemulsion.

30. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the bisphosphonate has the formula II



II

wherein

R^4 is H, OH or Cl, and

R^5 is

- (a) alkyl with 1 to 6 carbon atoms, optionally substituted with amino, alkylamino, dialkylamino or heterocyclyl;
- (b) halogen;
- (c) arylthio or chlorosubstituted arylthio;
- (d) cycloalkylamino with 5 to 7 carbons; or
- (e) saturated five or six membered nitrogen containing, heterocyclyl with 1 or 2 heteroatoms.

31. (Previously presented) The pharmaceutical formulation according to claim 30 wherein the bisphosphonate has the formula II wherein

R^4 is H or OH and

R^5 is

- (a) alkyl with 1 to 6 carbon atoms, optionally substituted with amino, alkylamino, dialkylamino, or heterocyclyl;
- (d) cycloalkylamino with 5 to 7 carbons; or

(e) saturated five or six membered nitrogen containing heterocyclyl with 1 or 2 heteroatoms.

32. (Previously presented) The pharmaceutical formulation according to claim 30 wherein the bisphosphonate has

the formula II wherein

R⁴ is OH and

R⁵ is

(a) alkyl with 1 to 6 carbon atoms, optionally substituted with amino, alkylamino, dialkylamino or heterocyclyl;

(d) cycloalkylamino with 5 to 7 carbons; or

(e) saturated five or six membered nitrogen containing heterocyclyl with 1 or 2 heteroatoms.

33. (Previously presented) The pharmaceutical formulation according to claim 30 wherein the bisphosphonate is

selected from the group consisting of:

4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid (alendronate),

N,N-dimethyl-3-amino-1-hydroxypropylidene-1,1-bisphosphonic acid (mildronate, olpadronate),

1-hydroxy-3-(N-methyl-N-pentylamino)propylidene-1,1-bisphosphonic acid (ibandronate),

1-hydroxy-2-(3-pyridyl)ethylidene-1,1-bisphosphonic acid (risedronate),

1-hydroxyethylidene-1,1-bisphosphonic acid (etidronate),

1-hydroxy-3-(1-pyrrolidinyl)propylidene-1,1-bisphosphonic acid,

1-hydroxy-2-(1-imidazolyl)ethylidene-1,1-bisphosphonic acid (zoledronate),
1-hydroxy-2-(imidazo[1,2-a]pyridin-3-yl)ethylidene-1,1-bisphosphonic acid
(minodronate),
1-(4-chlorophenylthio)methylidene-1,1-bisphosphonic acid (tiludronate),
1-(cycloheptylamino)methylidene-1,1-bisphosphonic acid (cimadronate, incadronate),
6-amino-1-hydroxyhexylidene-1,1-bisphosphonic acid (neridronate) and
pharmaceutically acceptable salts thereof.

34. (Previously presented) The pharmaceutical formulation according to claim 33 wherein the bisphosphonate is alendronate (4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid) or a pharmaceutically acceptable salt thereof.

Claims 35-38 (Canceled)

39. (Previously presented) The pharmaceutical formulation according to any one of claims 1 to 34, wherein the formulation is in particulate form.
40. (Previously presented) The pharmaceutical formulation according to claim 39 wherein the particulate form is solid or semisolid.
41. (Previously presented) The pharmaceutical formulation according to claim 39 or 40, wherein the bisphosphonate is in the form of micronized powder.
42. (Previously presented) A process for the preparation of a pharmaceutical formulation according to any one of claims 1 to 34, comprising forming a mixture of (i) at least one bisphosphonate, (ii) an additive and (iii) a pharmaceutically acceptable carrier.

Claim 43 (Canceled)

Claim 44 (Canceled)

45. (Previously presented) A method for inhibiting bone resorption which comprises administering to a mammal in need of such treatment an effective amount of a pharmaceutical formulation according to any one of claims 1 to 34.
46. (Previously presented) A method for treating or preventing osteoporosis and bone loss related to age, steroid therapy, rheumatism, Paget's disease, cancer, secondary osteoporosis except steroid induced osteoporosis, periodontitis or osteoarthritis, which comprises administering to a mammal in need of such treatment an effective amount of a pharmaceutical formulation according to any one of claims 1 to 34.
47. (Previously presented) The pharmaceutical formulation according to claim 1, wherein the additive is a phosphonate derivative selected from the group consisting of DL- α -glycerophosphate, 3-amino-1-hydroxypropylidene-1,1-diphosphonate, diethyl maleate and diethylethoxymethylene malonate.